

## Isolation, Structure Determination, and Total Synthesis of the Dibenzofurans $\alpha$ - and $\beta$ -Pyrufuran, New Phytoalexins from the Wood of *Pyrus communis* L.

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The antifungal compounds  $\alpha$ - and  $\beta$ -pyrufuran have been isolated from the wood of perry pear trees [*Pyrus communis* L. (Rosaceae), cv. Hendre Huffcap) infected with *Chondrostereum purpureum* (Pers. ex Fr.) Pouzar, the causative fungus of silver leaf disease. Spectroscopic and chemical evidence show that the compounds are 1,2,3,4-substituted trimethoxydibenzofuranols. Three of the four possible positional isomers, compounds (11), (12), and (13), have been synthesized by cyclisation of the corresponding trimethoxydiphenyl ethers using palladium(II) acetate, followed by oxidation of the organo-lithium derivative using lithium *t*-butyl peroxide. The latter stage proved unsuccessful in the attempted synthesis of 2,3,4-trimethoxydibenzofuran-1-ol (10). Comparison of spectroscopic and chromatographic properties of the natural products and synthesized compounds show  $\alpha$ -pyrufuran and  $\beta$ -pyrufuran to be 1,3,4-trimethoxydibenzofuran-2-ol (11) and 1,2,4-trimethoxydibenzofuran-3-ol (12), respectively.

The generation of antimicrobial phenolic compounds by parenchyma cells in xylem has been recognised as a part of the natural defence mechanism of trees against fungal attack.<sup>1-3</sup> This process can take place both during the transformation of sapwood to heartwood and as an active response of sapwood to infection.<sup>4-6</sup> Both processes are associated with cell death. In the second process the phenolic compounds accumulate in a zone of pigmented tissues surrounding the infected decay column.<sup>4,7</sup> We now report the isolation, identification, and total synthesis of the two dibenzofurans  $\alpha$ - and  $\beta$ -pyrufuran, phytoalexins isolated from a narrow dark pigmented reaction zone between healthy and silver leaf (*Chondrostereum purpureum*)-infected sapwood of perry pear (*Pyrus communis* cv. Hendre Huffcap).

$\alpha$ - and  $\beta$ -Pyrufuran were found in a common fraction from adsorption chromatography of ethanolic extracts of sapwood of perry pear which contained infections of silver leaf. The two isomers were separated by reverse-phase h.p.l.c.

The pure non-crystalline compounds both gave a mass spectrum (e.i.) (electron impact) which exhibited a molecular ion [ $C_{15}H_{14}O_5$ ]<sup>+</sup> and a base peak [ $M - Me$ ]<sup>+</sup> [ $C_{14}H_{11}O_5$ ]<sup>+</sup>. Chemical ionisation (isobutane) produced [ $M + H$ ]<sup>+</sup> peaks at  $m/z$  275. The <sup>1</sup>H n.m.r. spectra were also very similar to each other. Both showed signals assignable to three methoxy groups ( $\delta$  3.92–4.19, 3  $\times$  3 H, 3  $\times$  s), a replaceable proton, probably hydroxy ( $\delta$  ca. 5.8 [CDCl<sub>3</sub>],  $\delta$  8.0 [(CD<sub>3</sub>)<sub>2</sub>CO], 1 H, br s), and 4 aromatic protons ( $\delta$  7.20–7.62, 3 H, m, and  $\delta$  7.94–8.13, 1 H, m). The i.r. spectra supported these observations, absorption bands being assignable to the same functional groups: OH (ca. 3 520 cm<sup>-1</sup>), aromatic (ca. 3 030w, ca. 1 600w, ca. 1 516m, ca. 1 503m), CH<sub>3</sub> (2 937m, ca. 2 833w), and C–O (ca. 1 060s, ca. 1 040s). There was no signal assignable to carbonyl.

Methylation (diazomethane) of  $\alpha$ - and  $\beta$ -pyrufuran produced an identical product, indistinguishable by m.s., <sup>1</sup>H and <sup>13</sup>C n.m.r., i.r., and u.v. spectroscopy, or by g.l.c. and t.l.c. characteristics. The mass spectrum gave a molecular ion at  $m/z$  288. The <sup>1</sup>H n.m.r. spectrum showed the presence of four methoxy groups ( $\delta$  3.96, 4.01, 4.08, and 4.16, 4  $\times$  3 H, 4  $\times$  s) and four aromatic protons ( $\delta$  7.18–7.65, 3 H, m, and  $\delta$  7.97–8.15, 1 H, m).

From this information it was deduced that  $\alpha$ - and  $\beta$ -pyrufuran were positional isomers in which one of three methoxy groups and a hydroxy group were transposed. Furthermore, the common molecular skeleton comprised a

C<sub>12</sub>O moiety in which there were nine double-bond equivalents, the oxygen atom existing as an ether linkage.

The proton-noise-decoupled <sup>13</sup>C n.m.r. spectra of  $\alpha$ - and  $\beta$ -pyrufuran and their methylation product showed twelve resonances in the range  $\delta_c$  110–156 p.p.m., four of which gave a positive nuclear Overhauser effect (n.O.e.), indicative of a heteroaromatic structure of twelve carbon atoms, four of which were directly bonded to hydrogen.

Signals of medium intensity in the range  $\delta_c$  60–62 p.p.m. corresponded to methoxy groups; three in the pyrufurans, four in the methylated product. The <sup>1</sup>H n.m.r. spectra of these compounds displayed chemical shifts and splitting patterns in the aromatic region characteristic of dibenzofuran (cf. ref. 8). In the case of tetra-substituted dibenzofurans only 1,2,3,4-substitution produces such a pattern, those of other substitutions being much simpler.

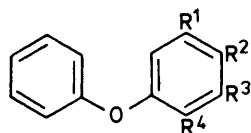
Methods of synthesizing 1,2,3,4-tetramethoxydibenzofuran (14) were now considered. Several methods of dibenzofuran synthesis have been reported, but all have disadvantages.<sup>9</sup> Classical methods include the Pschorr cyclisation of 2-phenoxyanilines,<sup>10-12</sup> and the cyclisation of 2,2'-dihydroxybiphenyls or their methyl esters.<sup>10,13-15</sup> Yields for the Pschorr cyclisation are reported to be relatively low and synthesis of 1,2,3,4-tetramethoxydibenzofuran (14) by either of these routes would require heavily substituted intermediates which are susceptible to oxidative decomposition. Dibenzofurans have recently been synthesized both by the annulation of benzofurans,<sup>9,16-18</sup> and by the palladium(II) acetate-promoted non-phenolic oxidative cyclisation of diphenyl ethers.<sup>19-22</sup> We have now synthesized 1,2,3,4-tetramethoxydibenzofuran (14) from 2,3,4,5-tetramethoxydiphenyl ether (5) by this latter method. Excess of palladium(II) acetate was used under nitrogen to prevent the formation of oxidation by-products. The nature of the solvent is important in determining both the rate of reaction and overall yield. In acetic acid the maximum yield obtained was 15% by refluxing for 15 h. In trifluoroacetic acid the reaction was complete after 3 h reflux and the yield was 65%. The product was found to be identical to the common methylation product of the pyrufurans, confirming that  $\alpha$ - and  $\beta$ -pyrufuran were 1,2,3,4-substituted trimethoxydibenzofuranols (10), (11), (12), or (13).

The <sup>13</sup>C nuclear magnetic resonances of the unsubstituted aromatic ring and the 9b carbon atom of the substituted ring in the pyrufurans and 1,2,3,4-tetramethoxydibenzofuran (14) were assigned by comparison of their spectra with that of

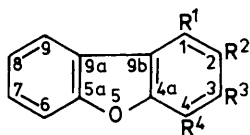
**Table.**  $^{13}\text{C}$  Chemical shifts ( $\delta/\text{p.p.m.}$ ) of dibenzofuran,<sup>8,23</sup> 1,2,3,4-tetramethoxydibenzofuran, and  $\alpha$ - and  $\beta$ -pyrufuran in  $\text{CDCl}_3$  and observed shifts on methylation of the pyrufurans

C atom	Dibenzofuran		$\alpha$ -Pyrufuran	(Shift)	$\beta$ -Pyrufuran	(Shift)
	Unsubstituted	(MeO) <sub>4</sub>				
5a	156.30	156.08	156.03	(+0.05)	155.77	(+0.31)
6 <sup>a</sup>	111.65	111.33	111.32	(+0.01)	111.19	(+0.14)
7 <sup>a</sup>	127.08	126.28	126.27	(+0.01)	125.68	(+0.60)
8 <sup>a</sup>	122.70	122.98	122.82	(+0.16)	123.02	(-0.04)
9 <sup>a</sup>	120.60	122.38	122.43	(-0.05)	121.91	(+0.47)
9a	124.30	123.41	123.28	(+0.13)	123.54	(-0.13)
9b	124.30	114.09	114.11	(-0.02)	110.54	(+3.55)

<sup>a</sup> Atoms whose signals have a positive n.O.e.



	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>
(1)	H	OMe	OMe	OMe
(2)	OMe	H	OMe	OMe
(3)	OMe	OMe	H	OMe
(4)	OMe	OMe	OMe	H
(5)	OMe	OMe	OMe	OMe



	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>
(6)	H	OMe	OMe	OMe
(7)	OMe	H	OMe	OMe
(8)	OMe	OMe	H	OMe
(9)	OMe	OMe	OMe	H
(10)	OH	OMe	OMe	OMe
(11)	OMe	OH	OMe	OMe
(12)	OMe	OMe	OH	OMe
(13)	OMe	OMe	OMe	OH
(14)	OMe	OMe	OMe	OMe

dibenzofuran<sup>8,23</sup> (Table). These signals gave some indication of the position of the hydroxy group in  $\alpha$ - and  $\beta$ -pyrufuran. Methylation of  $\beta$ -pyrufuran noticeably deshielded carbon atoms 5a, 7, 9, and 9b, and shielded or weakly deshielded carbon atoms 6, 8, and 9a. In the case of  $\alpha$ -pyrufuran the shifts were smaller and the overall pattern was reversed. These changes were attributed primarily to mesomeric effects and indicated that the hydroxy group in  $\alpha$ -pyrufuran was *meta* to atom 9b, *i.e.* in positions 2 or 4 [compound (11) or (13)] whereas in  $\beta$ -pyrufuran the hydroxy group was *ortho* or *para* to atom 9b, *i.e.* in the 1 or 3 position [compound (10) or (12)].

Evidence unequivocally establishing the position of the hydroxy group in  $\alpha$ - and  $\beta$ -pyrufuran was now obtained by total synthesis. The simplest unambiguous route to the 1,2,3,4-trimethoxydibenzofuranols (10)–(13) appeared to be from the corresponding trimethoxydiphenyl ethers (1)–(4) *via* the trimethoxydibenzofurans (6)–(9). The trimethoxydiphenyl

ethers were prepared in 50–80% yields by a solvent-assisted Ullmann synthesis.<sup>24</sup> These were cyclised to the corresponding dibenzofurans in 24–64% yields by reaction with excess of palladium(II) acetate in refluxing 40% trifluoroacetic acid-acetic acid under nitrogen. Lithiation of resorcinol ethers takes place at the 2-position,<sup>25</sup> and 3,5-dimethoxybiphenyls have been successfully hydroxylated at the 4-position by lithiation followed by oxidation with the lithium salt of *t*-butyl hydroperoxide.<sup>26</sup> Hydroxylation of the trimethoxydibenzofurans (6)–(9) was attempted using this method. 1,3,4-Trimethoxydibenzofuran-2-ol (11), 1,2,4-trimethoxydibenzofuran-3-ol (12), and 1,2,3-trimethoxydibenzofuran-4-ol (13) were successfully synthesized, but in low yields (5–17%) with more than 70% of starting material remaining. In the case of 2,3,4-trimethoxydibenzofuran (6) no corresponding dibenzofuran-1-ol (10) or dibenzofuran-6-ol was isolated and more than 80% of the starting material was recovered. A possible explanation for this observation was that lithiation had taken place at position 1, as might be expected since 2-methoxydibenzofuran is lithiated at this position in preference to position 6;<sup>10</sup> subsequent oxidation might then have failed because of steric effects (*cf.* ref. 27).

A comparison of the spectroscopic (m.s.,  $^1\text{H}$  n.m.r., i.r., and u.v.) and chromatographic (g.l.c., t.l.c., and h.p.l.c.) properties of the synthetic compounds with those of the natural ones showed that  $\alpha$ -pyrufuran was 1,3,4-trimethoxydibenzofuran-2-ol (11) and  $\beta$ -pyrufuran was 1,2,4-trimethoxydibenzofuran-3-ol (12). Dibenzofurans are comparatively rare natural products. Thirteen have been identified in lichens,<sup>28–32</sup> but only five have previously been reported from three species of higher plants.<sup>13,33–35</sup>  $\alpha$ - and  $\beta$ -Pyrufuran are the first natural dibenzofurans to be reported with a 1,2,3,4-substitution pattern; they are also the first to be reported in which neither aromatic ring is alkylated.

T.l.c. plate bioassays<sup>36</sup> against *Cladosporium cucumerinum* showed that the pyrufurans were the principal antifungal components in ethanolic extracts of perry pear sapwood. G.l.c. and h.p.l.c. analysis of these extracts showed that the pyrufurans occurred at concentrations of  $<50 \mu\text{g g}^{-1}$  fresh weight in healthy wood and *ca.*  $500 \mu\text{g g}^{-1}$  in infected wood, but at the edge of infection in a narrow dark pigmented zone concentrations of *ca.*  $5000 \mu\text{g g}^{-1}$  were found. The biological activity, biosynthesis, accumulation, and metabolism of these compounds in relation to disease resistance are currently being investigated and findings will be published elsewhere.

## Experimental

Accurate molecular masses were determined using a Kratos MS 30 mass spectrometer with electron-impact ionisation.

Chemical-ionisation (isobutane, *ca.* 0.3 Torr) and electron-impact mass spectra were measured from direct insertion probe samples on a Finnigan 4021 MS-DS.  $^1\text{H}$  90-MHz,  $^1\text{H}$  200-MHz, and  $^{13}\text{C}$  90-MHz n.m.r. spectra were recorded on Perkin-Elmer R32, JEOL FX 200, and JEOL FX 90Q instruments, respectively. M.p.s were measured on a Kofler block and are uncorrected. Kieselgel 40 (Merck: 70–230 mesh), and 'SilicAR' CC-4 (Mallinckrodt 100 mesh) were used for column chromatography. T.l.c. was done on pre-coated Kieselgel 60 F<sub>254</sub> plates (Merck: 0.25 mm). G.l.c. was on a 2 m × 2 mm i.d. glass column packed with 3% OV 225 on 80–100 mesh Gas-Chrom Q at 225 °C using N<sub>2</sub> carrier at a flow rate of 30 ml min<sup>-1</sup>. Reverse-phase h.p.l.c. was done on a Hypersil ODS 25 cm × 4.6 mm i.d. analytical column eluted with methanol–water–acetic acid (65:34:1 v/v/v) at a flow rate of 0.6 ml min<sup>-1</sup> at 30 °C (System 1) and an Apex ODS 15 cm × 1 cm i.d. semi-preparative column eluted with 30% water–methanol at 25 °C (System 2). Biological activity was detected by a t.l.c. *Cladosporium cucumerinum* bioassay<sup>36</sup> using a 5% ethanol–chloroform solvent system.

**Isolation of  $\alpha$ - and  $\beta$ -Pyrufuran.**—A log (14 cm diameter × 40 cm) heavily infected with *Chondrostereum purpureum* was cut from a perry pear tree (*Pyrus communis* L. cv. Herfdre Huffcap). The bark and cambium were discarded and the wood was planed into thin shavings. The shavings (2 kg) were soaked in ethanol at 20 °C for 5 d. The ethanol was removed from the extract under reduced pressure (*ca.* 40 °C) and the residue was washed with ethyl acetate (5 × 250 ml). The ethyl acetate-soluble extract was chromatographed on a column (60 cm × 3 cm i.d.) of Kieselgel 40 eluted with 20% ethyl acetate–*n*-hexane. The first biologically active fraction was further purified by chromatography on a column (60 cm × 3 cm i.d.) of 'SilicAR' CC-4 eluted with toluene. A fraction (220 mg) was isolated which gave a single sharp peak on g.l.c. ( $R_f$  5.7 min) and a single spot on t.l.c. (1.5% EtOH–CHCl<sub>3</sub>,  $R_F$  0.39; 20% acetone–*n*-hexane,  $R_F$  0.22). Reverse-phase h.p.l.c. (System 1) resolved the fraction into  $\alpha$ - and  $\beta$ -pyrufuran ( $R_f$  23.4 min and 25.4 min, respectively). Samples of  $\alpha$ - and  $\beta$ -pyrufuran were obtained by collecting fractions ( $R_f$  22.4–24 min and 25.7–29 min) from repeated injections of the mixture into this h.p.l.c. system.\* The fractions were each evaporated to dryness and dissolved in diethyl ether, (50 ml), and the solutions were washed with water (2 × 50 ml) and further purified by t.l.c. using 5% EtOH–CHCl<sub>3</sub> as eluant. In each case the band at  $R_F$  0.65 (quenches u.v. 254 nm) was extracted with diethyl ether, and the solvent was removed under reduced pressure at 25 °C.  $\alpha$ - and  $\beta$ -Pyrufuran were obtained as oils.

**$\alpha$ -Pyrufuran**, (63 mg) [Found:  $M^+$ , 274.0826. C<sub>15</sub>H<sub>14</sub>O<sub>5</sub> requires  $M$ , 274.0841; ( $M - \text{Me}$ )<sup>+</sup>, 259.0589. C<sub>14</sub>H<sub>11</sub>O<sub>5</sub> requires  $m/z$ , 259.0606];  $\lambda_{\text{max}}$  (EtOH; 1 cm) 224 [log<sub>10</sub> ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) 4.44], 259 (4.07), 287 (4.23), and 315sh nm (3.46);  $\nu_{\text{max}}$  (CHCl<sub>3</sub>; 0.1 mm) 3 530m (OH), 3 050w, 3 030w, 3 000w (Ar), 2 937m, 2 836w (CH<sub>3</sub>), 1 603w, 1 518m, 1 505m (Ar), 1 457m, 1 425s, 1 412s (Ar and CH<sub>3</sub>), 1 372m, 1 297m, 1 265s, 1 065s, and 1 045s cm<sup>-1</sup> (C–OH, and C–O–C); (KBr disc) additional  $\nu_{\text{max}}$  at 3 400s br (bonded OH), 1 224s (C–O), and 750s cm<sup>-1</sup> (4 adjacent Ar–H);  $\delta_{\text{H}}$  [200 MHz; (CD<sub>3</sub>)<sub>2</sub>CO; Me<sub>4</sub>Si] 3.95, 4.04, and 4.12 (each 3 H, s, together 1-, 3-, and 4-OMe), 7.31–7.39 (1 H, m, 8-H), 7.41–7.49 (1 H, m, 7-H), 7.56–7.61 (1 H, m, 6-H), 7.81 (1 H, s, 2-OH), 8.05–8.10 (1 H, m, 9-H); full analysis of the second-order spectrum gave  $\delta_{\text{H}}$  7.35 (1 H, ddd,  $J$  7.8, 7.4, and 0.9 Hz, 8-H),

7.45 (1 H, ddd,  $J$  8.3, 7.4, and 1.3 Hz, 7-H), 7.59 (1 H, ddd,  $J$  8.3, 0.9, and 0.6 Hz, 6-H), and 8.07 (1 H, ddd,  $J$  7.8, 1.3, and 0.6 Hz, 9-H);  $\delta_{\text{H}}$  (90 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 4.04, 4.06, and 4.16 (each 3 H, s, together 1-, 3-, and 4-OMe), 5.60 (1 H, s, 2-OH), 7.20–7.60 (3 H, m, 6-, 7-, and 8-H), and 7.96–8.13 (1 H, m, 9-H);  $\delta_{\text{C}}$  (90 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 60.76, 61.22, and 61.80 (together 1-, 3-, and 4-OMe), 111.32 (C-6), 114.11 (C-9b), 122.43 (C-9), 122.82 (C-8), 123.28 (C-9a), 126.27 (C-7), 134.52, 136.27, 138.03, 139.46, and 141.47 (together C-1, -2, -3, -4, and -4a), and 156.03 p.p.m. (C-5a);  $m/z$  (e.i., 40 eV) 275 (12.8%), 274 ( $M^+$ , 85.8), 260 (14.2), 259 (100), 244 (10.6), 216 (44.1), 213 (20.4), 201 (42.2), 173 (31.0), 145 (18.1), 144 (14.6), 137 (21.2), 128 (11.8), 117 (11.0), 101 (16.3), 89 (35.8), and 88 (26.5);  $m/z$  (c.i., isobutane; 0.3 Torr) 276 (13.4%), 275 ( $M + \text{H}^+$ , 100), and 274 (17.8);  $R_F$  (1.5% EtOH–CHCl<sub>3</sub>) 0.38, [20% (CH<sub>3</sub>)<sub>2</sub>CO–*n*-C<sub>6</sub>H<sub>14</sub>] 0.23;  $R_f$  g.l.c. 7.3 min;  $R_f$  h.p.l.c. (System 1) 23.4 min.

**$\beta$ -Pyrufuran**, (45 mg) [Found:  $M^+$ , 274.0809. C<sub>15</sub>H<sub>14</sub>O<sub>5</sub> requires  $M$ , 274.0841; ( $M - \text{Me}$ )<sup>+</sup>, 259.0599. C<sub>14</sub>H<sub>11</sub>O<sub>5</sub> requires  $m/z$  259.0606];  $\lambda_{\text{max}}$  (EtOH; 1 cm) 217 (log  $\epsilon$  4.51), 227 (4.49), 261 (4.05), 289 (4.24), and 301sh nm (4.05);  $\nu_{\text{max}}$  (CHCl<sub>3</sub>; 0.1 mm) 3 518m (OH), 3 050w, 3 030w, 3 005w (Ar), 2 937m, 2 830w (CH<sub>3</sub>), 1 660w, 1 630w, 1 602w, 1 515m, 1 502m (Ar), 1 460m, 1 450s, 1 412s (Ar and CH<sub>3</sub>), 1 347m, 1 300m, 1 267m, 1 060s, and 1 040s cm<sup>-1</sup> (C–OH, and C–O–C); (KBr disc) additional  $\nu_{\text{max}}$  at 3 400s br (bonded OH), 1 224s (C–O), and 750s cm<sup>-1</sup> (4 adjacent Ar–H);  $\delta_{\text{H}}$  [200 MHz; (CD<sub>3</sub>)<sub>2</sub>CO; Me<sub>4</sub>Si] 3.92, 4.06, and 4.07 (each 3 H, s, together 1-, 2-, and 4-OMe), 7.30–7.45 (2 H, m, 7- and 8-H), 7.55–7.60 (1 H, m, 6-H), 7.99–8.04 (1 H, m, 9-H), and 8.25 (1 H, s, 3-OH); full analysis of the second-order spectrum gave  $\delta_{\text{H}}$  7.34 (1 H, ddd,  $J$  7.8, 7.5, and 0.5 Hz, 8-H), 7.41 (1 H, ddd,  $J$  8.2, 7.5, and 1.2 Hz, 7-H), 7.57 (1 H, ddd,  $J$  8.2, 0.5 and 0.3 Hz, 6-H), and 8.02 (ddd,  $J$  7.8, 1.2 and 0.3 Hz, 9-H);  $\delta_{\text{H}}$  (90 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 4.01, 4.07, and 4.19 (each 3 H, s, together 1-, 2-, and 4-OMe), 6.02 (1 H, s, 3-OH), 7.24–7.62 (3 H, m, 6-, 7-, and 8-H), and 7.94–8.13 (1 H, m, 9-H);  $\delta_{\text{C}}$  (90 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 60.89, 61.22, and 61.54 (together 1-, 2-, and 4-OMe), 110.54 (C-9b), 111.19 (C-6), 121.91 (C-9), 123.02 (C-8), 123.54 (C-9a), 125.68 (C-7), 129.00, 136.73, 141.47, 142.71, and 143.94 (together C-1, -2, -3, -4, and -4a), and 155.77 p.p.m. (C-5a);  $m/z$  (e.i., 40 eV) 275 (16.8%), 274 ( $M^+$ , 96.6), 260 (16.8), 259 (100), 244 (14.7), 216 (53.6), 213 (29.3), 201 (53.6), 173 (42.6), 145 (27.5), 144 (17.9), 137 (26.8), 128 (15.5), 117 (15.2), 101 (22.3), 89 (51.8), and 88 (35.7);  $m/z$  (c.i., isobutane; 0.3 Torr) 276 (11.9%), 275 ( $M + \text{H}^+$ , 100), and 274 (10.3);  $R_F$  (1.5% EtOH–CHCl<sub>3</sub>) 0.41, [20% (CH<sub>3</sub>)<sub>2</sub>CO–*n*-C<sub>6</sub>H<sub>14</sub>] 0.22;  $R_f$  g.l.c. 7.3 min;  $R_f$  h.p.l.c. (System 1) 25.4 min.

**Methylation of  $\alpha$ - and  $\beta$ -Pyrufuran.**— $\alpha$ - and  $\beta$ -Pyrufuran (20 mg) were quantitatively methylated by the addition of excess of diazomethane in diethyl ether (5 ml). The common methylation product 1,2,3,4-tetramethoxydibenzofuran (14) was isolated as an oil by t.l.c. (1.5% EtOH–CHCl<sub>3</sub>) and had  $\lambda_{\text{max}}$  (EtOH; 1 cm) 220sh (log  $\epsilon$  4.56), 229 (4.60), 261 (4.21), 285 (4.34), 297sh (3.92), and 309sh nm (3.75);  $\nu_{\text{max}}$  (CHCl<sub>3</sub>; 0.1 mm) 3 050w, 3 020w, 3 000w (Ar), 2 930m, 2 825w (CH<sub>3</sub>), 1 597w, 1 494m (Ar), 1 457m, 1 448s, 1 416m, 1 398s (Ar and CH<sub>3</sub>), 1 296m, 1 070s, and 1 050s cm<sup>-1</sup> (C–O–C);  $\delta_{\text{H}}$  (90 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 3.96, 4.01, 4.07, and 4.15 (each 3 H, s, together 1-, 2-, 3-, and 4-OMe), 7.20–7.63 (3 H, m, 6-, 7-, and 8-H), and 7.98–8.13 (1 H, m, 9-H);  $\delta_{\text{C}}$  (90 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 61.05, 61.44, 61.76, and 61.92 (together 1-, 2-, 3-, and 4-OMe), 111.33 (C-6), 114.10 (C-9b), 122.38 (C-9), 122.98 (C-8), 123.41 (C-9a), 126.33 (C-7), 135.17, 142.49, 143.16, 145.93, and 150.42 (together C-1, -2, -3, -4, and -4a), and 156.08 p.p.m. (C-5a);  $m/z$  (e.i., 40 eV) 289 (19.2%), 288 ( $M^+$ , 100), 273

\* We have since separated the pyrufurans more efficiently by t.l.c. of the acetylated derivatives [eluant 10% (CH<sub>3</sub>)<sub>2</sub>CO–*n*-C<sub>6</sub>H<sub>14</sub> × 2].

(88.2), 243 (16.6), 230 (36.3), 215 (41.9), 187 (31.8), 144 (81.9), and 88 (45.8);  $R_F$  (1.5% EtOH-CHCl<sub>3</sub>) 0.65, [20% (CH<sub>3</sub>)<sub>2</sub>CO-n-C<sub>6</sub>H<sub>14</sub>] 0.54;  $R_t$  g.l.c. 3.6 min. See also below.

*Tetra- and Trimethoxydiphenyl Ethers.*—2,3,4,5-Tetramethoxydiphenyl ether (5) and 2,3,4-, 2,3,5- and 2,4,5-trimethoxydiphenyl ether (1), (2), and (3) were prepared from the corresponding tetramethoxy- and trimethoxy-bromobenzenes<sup>37</sup> by a solvent-assisted, copper(I)-catalysed Ullmann condensation<sup>24</sup> with phenol. The reaction mixture was kept throughout under dry nitrogen. Freshly cut sodium (0.33 g, 0.014 mol) was added to dry methanol (20 ml), followed by dry benzene (20 ml) and phenol (2.82 g, 0.03 mol). The methanol and benzene were distilled off to leave the dry sodium phenate salt in an excess of phenol, to which dry pyridine (35 ml) was added. The mixture was heated to boiling point and the methoxy-substituted bromobenzene (0.015 mol) and anhydrous copper(I) chloride (0.1 g) were added. The mixture was refluxed for 20–40 h, the reaction being monitored by t.l.c. (1.5% EtOH-CHCl<sub>3</sub>). The mixture was then poured into water (100 ml), and acidified with hydrochloric acid, and the products were extracted with diethyl ether (3 × 30 ml). The extract was washed in turn with hydrochloric acid (10% w/v; 2 × 100 ml), aqueous sodium hydroxide (5% w/v; 2 × 100 ml), and water (2 × 200 ml). The solvent was removed by evaporation under reduced pressure and the remaining product was purified by column chromatography (Kieselgel 40; 40 cm × 2.5 cm i.d.; eluant 50% CHCl<sub>3</sub>-n-C<sub>6</sub>H<sub>14</sub>). 3,4,5-Trimethoxydiphenyl ether (4) was similarly prepared from 3,4,5-trimethoxyphenol (2.76 g, 0.015 mol) and bromobenzene (5.52 g, 0.03 mol).

2,3,4,5-Tetramethoxydiphenyl ether (5) (2.19 g, 50% after 40 h) was obtained as an oil (Found:  $M^+$ , 290.1121. C<sub>16</sub>H<sub>18</sub>O<sub>5</sub> requires  $M$ , 290.1154);  $\lambda_{max}$  (EtOH; 1 cm) 210 (log  $\epsilon$  4.36), 263 (3.14), 271 (3.30), and 277 nm (3.36);  $\nu_{max}$  (CHCl<sub>3</sub>; 0.1 mm) 3 070w, 3 020w, 3 000m (Ar), 2 930m, 2 840w (CH<sub>3</sub>), 1 587m, 1 484s (Ar), 1 467s, 1 445m, 1 427m, 1 410s (Ar and CH<sub>3</sub>), 1 127s, 1 090s, and 1 038s cm<sup>-1</sup> (C-O-C);  $\delta_H$  (90 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 3.69, 3.72, 3.84, and 3.92 (each 3-H, s, together 2-, 3-, 4-, and 5-OMe), 6.32 (1 H, s, 6-H), and 6.82–7.50 (5 H, m, 2', 3', 4', 5', and 6'-H);  $m/z$  (e.i., 40 eV) 291 (18.5%), 290 ( $M^+$ , 100), 276 (13.4), 275 (74.8), 247 (16.5), 232 (25.6), 217 (11.8), 189 (25.0), 91 (11.2), 77 (40.4), and 69 (16.1);  $R_F$  (1.5% EtOH-CHCl<sub>3</sub>) 0.63, [20% (CH<sub>3</sub>)<sub>2</sub>CO-n-C<sub>6</sub>H<sub>14</sub>] 0.42;  $R_t$  g.l.c. (190 °C) 8.8 min.

2,3,4-Trimethoxydiphenyl ether (1) (2.14 g, 55% after 24 h) was obtained as rhombic plates, m.p. 57–60 °C (from 50% n-C<sub>6</sub>H<sub>14</sub>-diethyl ether) (lit.<sup>38</sup> 56–58 °C) (Found:  $M^+$ , 260.1015. Calc. for C<sub>15</sub>H<sub>16</sub>O<sub>4</sub>:  $M$ , 260.1049);  $\lambda_{max}$  (EtOH; 1 cm) 212 (log  $\epsilon$  4.33), 264sh (3.22), 270 (3.33), and 277 nm (3.34);  $\nu_{max}$  (CDCl<sub>3</sub>; 0.1 mm) 3 060w, 3 020w, 3 000m (Ar), 2 933m, 2 833w (CH<sub>3</sub>), 1 590m (Ar), 1 477s, 1 430m, 1 418m (Ar and CH<sub>3</sub>), 1 293m, 1 230s br, 1 093s, 1 043s, and 1 007m cm<sup>-1</sup> (C-O-C);  $\delta_H$  (90 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 3.84, 3.88, and 3.94 (each 3 H, s, together 2-, 3-, and 4-OMe), 6.56 and 6.75 (each 1 H, d,  $J$  9.2 Hz, together 5-, and 6-H), and 6.79–7.46 (5 H, m, 2', 3', 4', 5', and 6'-H);  $m/z$  (e.i., 40 eV) 261 (17.9%), 260 ( $M^+$ , 100), 245 (35.4), 185 (10.0), 131 (14.5), 124 (10.0), 105 (15.0), 91 (32.6), 77 (46.7), and 69 (18.1);  $R_F$  (1.5% EtOH-CHCl<sub>3</sub>) 0.64, [20% (CH<sub>3</sub>)<sub>2</sub>CO-n-C<sub>6</sub>H<sub>14</sub>] 0.45.

2,3,5-Trimethoxydiphenyl ether (2) (2.07 g, 53% after 20 h) was an oil (Found:  $M^+$ , 260.1027);  $\lambda_{max}$  (EtOH; 1 cm) 228 (log  $\epsilon$  4.55), 265sh (3.77), 272 (3.92), and 278 nm (3.98);  $\nu_{max}$  (CHCl<sub>3</sub>; 0.1 mm) 3 040w, 3 020w, 3 005m (Ar), 2 957w, 2 935m, 2 830w (CH<sub>3</sub>), 1 600m, 1 593s (Ar), 1 500s, 1 490s (Ar), 1 465m, 1 453m, 1 423m (Ar and CH<sub>3</sub>), 1 215m br, 1 146s, 1 090s, 1 050m, and 998m cm<sup>-1</sup> (C-O-C);  $\delta_H$  (90

MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 3.67, 3.75, and 3.85 (each 3 H, s, together 2-, 3-, and 5-OMe), 6.14 and 6.33 (each 1 H, d,  $J$  3 Hz, together 4-, and 6-H), and 6.40–7.50 (5 H, m, 2', 3', 4', 5', and 6'-H);  $m/z$  (e.i., 40 eV) 261 (15.8%), 260 ( $M^+$ , 100), 244 (13.5), 245 (92.8), 217 (40.3), 213 (13.2), 174 (10.4), 125 (22.0), 115 (11.7), 114 (17.4), 77 (35.7), and 69 (29.3);  $R_F$  (1.5% EtOH-CHCl<sub>3</sub>) 0.65, [20% (CH<sub>3</sub>)<sub>2</sub>CO-n-C<sub>6</sub>H<sub>14</sub>] 0.39.

2,4,5-Trimethoxydiphenyl ether (3) (3.08 g, 79% after 20 h) was an oil (Found:  $M^+$ , 260.1057);  $\lambda_{max}$  (EtOH; 1 cm) 211 (log  $\epsilon$  4.26), 273sh (3.50), 280sh (3.62), and 292 nm (3.77);  $\nu_{max}$  (CHCl<sub>3</sub>; 0.1 mm) 3 060w, 3 020w, 3 000m (Ar), 2 955w, 2 930w, 2 828w (CH<sub>3</sub>), 1 588m, 1 518s, 1 487s (Ar), 1 463s, 1 453m, 1 437m (Ar and CH<sub>3</sub>), 1 197s br, and 1 030s cm<sup>-1</sup> (C-O-C);  $\delta_H$  (90 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 3.77, 3.77, and 3.92 [each 3 H, s (2 degenerate), together 2-, 4-, and 5-OMe], 6.72 and 6.72 [each 1 H, s (degenerate), together 3- and 6-H], and 6.43–7.45 (5 H, m, 2', 3', 4', 5', and 6'-H);  $m/z$  (e.i., 40 eV) 261 (17.1%), 260 ( $M^+$ , 100), 245 (53.2), 217 (32.5), 125 (15.0), 124 (28.8), 123 (11.1), 109 (10.5), 77 (46.5), and 69 (29.0);  $R_F$  (1.5% EtOH-CHCl<sub>3</sub>) 0.64, [20% (CH<sub>3</sub>)<sub>2</sub>CO-n-C<sub>6</sub>H<sub>14</sub>] 0.29.

3,4,5-Trimethoxydiphenyl ether (4) (2.50 g, 64% after 20 h) was obtained as cubic prisms, m.p. 85–86.5 °C (from diethyl ether) (lit.<sup>38</sup> 84–86 °C) (Found:  $M^+$ , 260.1077);  $\lambda_{max}$  (EtOH; 1 cm) 216 (log  $\epsilon$  4.45), 238sh (3.98), 265 (3.33), 272 (3.35), and 278 nm (3.30);  $\nu_{max}$  (CHCl<sub>3</sub>; 0.1 mm) 3 060w, 3 020w, 3 000w (Ar), 2 958w, 2 930w, 2 825w (CH<sub>3</sub>), 1 588s, 1 500s, 1 485s (Ar), 1 465s, 1 447s, 1 430m, 1 415 (Ar and CH<sub>3</sub>), 1 215s br, 1 172m, 1 127s, 1 000s, and 989s cm<sup>-1</sup> (C-O-C);  $\delta_H$  (90 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 3.79 (6 H, s, 3- and 5-OMe), 3.82 (3 H, s, 4-OMe), 6.25 (2 H, s, 2- and 6-H), and 6.95–7.41 (5 H, m, 2', 3', 4', 5', and 6'-H);  $m/z$  (e.i., 40 eV) 261 (16.9%), 260 ( $M^+$ , 85.5), 244 (16.4), 245 (100), 217 (36.1), 187 (20.3), 161 (10.1), 131 (10.0), 115 (10.0), 77 (51.0), and 69 (20.0);  $R_F$  (1.5% EtOH-CHCl<sub>3</sub>) 0.61, [20% (CH<sub>3</sub>)<sub>2</sub>CO-n-C<sub>6</sub>H<sub>14</sub>] 0.40.

*Tetra- and Trimethoxydibenzofurans.*—A mixture of 2,3,4,5-tetramethoxydiphenyl ether (5) (0.725 g, 0.0025 mol) and palladium(II) acetate (1.12 g, 0.005 mol) in trifluoroacetic acid (50 ml) was refluxed under dry nitrogen until all the diphenyl ether was consumed (3 h). The reaction was monitored by g.l.c. The solvent was removed by distillation. The residue was dissolved in ethyl acetate (50 ml) and washed in turn with water (2 × 50 ml), 10% aqueous sodium hydrogen carbonate (2 × 50 ml), and water (2 × 50 ml). The ethyl acetate was removed under reduced pressure and the residue of 1,2,3,4-tetramethoxydibenzofuran (14) was purified by column chromatography (Mallinkrodt CC-4; 40 cm × 2.5 cm. i.d.; eluant toluene).

1,2,3-, 1,2,4-, 1,3,4-, and 2,3,4-trimethoxydibenzofuran (9), (8), (7), and (6) were similarly prepared from the corresponding diphenyl ethers and a 1.5-molar excess of palladium(II) acetate in 40% trifluoroacetic acid-acetic acid. They were purified by column chromatography (eluant 50% CHCl<sub>3</sub>-n-C<sub>6</sub>H<sub>14</sub>) with the exception of 2,3,4-trimethoxydibenzofuran (6) which was further purified by h.p.l.c. (System 2).

1,2,3,4-Tetramethoxydibenzofuran (14) (0.47 g, 65% after 3 h) was obtained as rhombic plates, m.p. 49–50 °C (from 50% n-C<sub>6</sub>H<sub>14</sub>-diethyl ether) (Found:  $M$ , 288.1011. C<sub>16</sub>H<sub>16</sub>O<sub>5</sub> requires  $M$ , 288.0997);  $\lambda_{max}$  (EtOH; 1 cm) 218sh (log  $\epsilon$  4.52), 227 (4.56), 260 (4.17), 284 (4.30), 294sh (3.89), and 307sh nm (3.71);  $\nu_{max}$  (CHCl<sub>3</sub>; 0.1 mm) 3 060w, 3 020w, 3 000w (Ar), 2 928m, 2 825w (CH<sub>3</sub>), 1 598w, 1 493m (Ar), 1 458m, 1 448s, 1 417m, 1 399s (Ar and CH<sub>3</sub>), 1 296m, 1 070s, and 1 051s

$\text{cm}^{-1}$  (C—O—C);  $\delta_{\text{H}}$  (90 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 3.97, 4.01, 4.08, and 4.15 (each 3 H, s, together 1-, 2-, 3-, and 4-OMe), 7.18—7.63 (3 H, m, 6-, 7-, and 8-H), and 7.98—8.13 (1 H, m, 9-H);  $\delta_{\text{C}}$  (90 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 61.05, 61.27, 61.38, and 61.76 (together 1-, 2-, 3-, and 4-OMe), 111.33 (C-6), 114.09 (C-9b), 122.38 (C-9), 122.98 (C-8), 123.41 (C-9a), 126.28 (C-7), 135.22, 142.53, 143.18, 145.95, 149.74 (together C-1, -2, -3, -4, and -4a) and 156.08 p.p.m. (C-5a);  $m/z$  (e.i., 40 eV) 289 (17.4%), 288 ( $M^+$ , 100), 273 (85.4), 243 (7.6), 230 (35.6), 215 (41.4), 187 (32.7), 144 (78.4), and 88 (50.8); chromatographic data were identical with those recorded above.

1,2,3-Trimethoxydibenzofuran (9) (0.41 g, 64% after 1 h) was obtained as rhombic plates, m.p. 42—43 °C (from diethyl ether) (Found:  $M^+$ , 258.0887.  $\text{C}_{15}\text{H}_{14}\text{O}_4$  requires  $M$ , 258.0892);  $\lambda_{\text{max}}$  (EtOH; 1 cm) 226 (log  $\epsilon$  4.56), 258 (4.15), 290 (4.32), and 298 nm (4.28);  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ; 0.1 mm) 3 060w, 3 020w, 3 002m (Ar), 2 960w, 2 935m, 2 835w ( $\text{CH}_3$ ), 1 632m, 1 598m, 1 490m (Ar), 1 475s, 1 462s, 1 449s, 1 427s, 1 416m (Ar and  $\text{CH}_3$ ), 1 350m, 1 303m, 1 245m, 1 190m, 1 170m, 1 143s, 1 107m, 1 090s, 1 057s, and 1 002m  $\text{cm}^{-1}$  (C—O—C);  $\delta_{\text{H}}$  (90 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 3.89, 3.92, and 4.12 (each 3 H, s, together 1-, 2-, and 3-OMe), 6.82 (1 H, s, 4-H), 7.18—7.55 (3 H, m, 6-, 7-, and 8-H), and 7.89—8.05 (1 H, m, 9-H);  $m/z$  (e.i., 40 eV) 259 (16.7%), 258 ( $M^+$ , 98.7), 244 (16.1), 243 (100), 215 (17.9), 200 (52.9), 186 (11.2), 185 (90.4), 183 (21.9), 155 (11.2), 139 (11.6), 129 (26.6), 113 (11.2), 101 (46.9), and 75 (12.9);  $R_{\text{F}}$  (1.5% EtOH— $\text{CHCl}_3$ ) 0.64, [20%  $(\text{CH}_3)_2\text{CO}$ — $n$ - $\text{C}_6\text{H}_{14}$ ] 0.52.

1,2,4-Trimethoxydibenzofuran (8) (0.30 g, 46% after 1.5 h) was obtained as rhombic plates, m.p. 112—113 °C (from diethyl ether) (Found:  $M^+$ , 258.0917);  $\lambda_{\text{max}}$  (EtOH; 1 cm) 220sh (log  $\epsilon$  4.44), 231 (4.50), 259 (4.13), 278sh (4.03), 283 (4.16), and 317 nm (3.63);  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ; 0.1 mm) 3 055w, 3 025w, 3 005m (Ar), 2 955w, 2 930m, 2 836m ( $\text{CH}_3$ ), 1 636w, 1 610m, 1 508s (Ar), 1 462m, 1 448s, 1 430m, 1 395m (Ar and  $\text{CH}_3$ ), 1 348m, 1 246s, 1 160s, 1 098m, 1 048m, and 1 028m (C—O—C);  $\delta_{\text{H}}$  (90 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 3.91, 3.99, and 4.01 (each 3 H, s, together 1-, 2-, and 4-OMe), 6.65 (1 H, s, 3-H), 7.18—7.63 (3 H, m, 6-, 7-, and 8-H), and 7.99—8.13 (1 H, m, 9-H);  $m/z$  (e.i., 40 eV) 259 (16.7%), 258 ( $M^+$ , 91.2), 244 (15.8), 243 (100), 215 (18.8), 200 (32.6), 185 (12.7), 184 (14.0), 142 (17.4), 129 (19.1), 114 (13.4), and 101 (11.2);  $R_{\text{F}}$  (1.5% EtOH— $\text{CHCl}_3$ ) 0.65, [20%  $(\text{CH}_3)_2\text{CO}$ — $n$ - $\text{C}_6\text{H}_{14}$ ] 0.42.

1,3,4-Trimethoxydibenzofuran (7) (0.30 g, 46% after 2.3 h) was obtained as rectangular prisms, m.p. 110—111.5 °C (from diethyl ether) (Found:  $M^+$ , 258.0923);  $\lambda_{\text{max}}$  (EtOH; 1 cm) 220 (log  $\epsilon$  4.59), 234 (4.58), 265 (4.23), 283 (4.30), 299 (4.05), and 310 (4.21);  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ; 0.1 mm) 3 050w, 3 025w, 3 005m (Ar), 2 959w, 2 935m, 2 837m ( $\text{CH}_3$ ), 1 635m, 1 602m, 1 513m (Ar), 1 463m, 1 452s, 1 434m, 1 395m (Ar and  $\text{CH}_3$ ), 1 334m, 1 250s, 1 102s, 1 075m, and 1 000m  $\text{cm}^{-1}$  (C—O—C);  $\delta_{\text{H}}$  (90 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 3.95, 3.98, and 4.05 (each 3 H, s, together 1-, 3-, and 4-OMe), 6.42 (1 H, s, 2-H), 7.14—7.56 (3 H, m, 6-, 7-, and 8-H), and 7.92—8.05 (1 H, m, 9-H);  $m/z$  (e.i., 40 eV) 259 (17.4%), 258 ( $M^+$ , 100), 243 (88.6), 215 (20.8), 200 (46.3), 184 (15.0), 142 (23.7), 129 (27.7), 114 (21.3), 113 (16.8), and 101 (15.7);  $R_{\text{F}}$  (1.5% EtOH— $\text{CHCl}_3$ ) 0.63, [20%  $(\text{CH}_3)_2\text{CO}$ — $n$ - $\text{C}_6\text{H}_{14}$ ] 0.38.

2,3,4-Trimethoxydibenzofuran (6) (0.15 g, 23% after 2.5 h), was an oil (Found:  $M^+$ , 258.0895);  $\lambda_{\text{max}}$  (EtOH; 1 cm) 233 (log  $\epsilon$  4.45), 256 (4.04), 290 (4.17), 297sh (4.09), and 316 nm (3.67);  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ; 0.1 mm) 3 060w, 3 025w, 3 000m (Ar), 2 932m, 2 828w ( $\text{CH}_3$ ), 1 595m, 1 490m (Ar), 1 475m, 1 462s, 1 438m, 1 423s (Ar and  $\text{CH}_3$ ), 1 358m, 1 187s, 1 120s, 1 095m, and 1 042s  $\text{cm}^{-1}$  (C—O—C);  $\delta_{\text{H}}$  (90 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 3.94, 3.95, and 4.22 (each 3 H, s, together 2-, 3-, and 4-OMe), 7.08 (1 H, s, 1-H), 7.15—7.63 (3 H, m, 6-, 7-, and 8-H), and 7.74—7.87 (1 H, m, 9-H);

$m/z$  (e.i., 40 eV) 259 (15.9%), 258 ( $M^+$ , 100), 244 (14.8), 243 (95.7), 215 (11.2), 200 (39.8), 185 (47.3), 183 (30.1), 155 (11.6), 139 (11.2), 129 (34.6), and 101 (34.8);  $R_{\text{F}}$  (1.5% EtOH— $\text{CHCl}_3$ ) 0.61, [20%  $(\text{CH}_3)_2\text{CO}$ — $n$ - $\text{C}_6\text{H}_{14}$ ] 0.42.

*Trimethoxydibenzofuranols.*—Trimethoxydibenzofurans (7), (8), and (9) were converted into the corresponding trimethoxydibenzofuranols (11), (12), and (13) by lithiation followed by reaction with the lithium salt of *t*-butyl peroxide, all reactions being conducted under dry nitrogen. A solution of *n*-butyllithium (0.64 g, 0.001 mol) in *n*-hexane (0.65 ml) was added to a solid  $\text{CO}_2$ -acetone-cooled solution of a trimethoxydibenzofuran (0.26 g, 0.001 mol) in sodium-dried diethyl ether (25 ml). The mixture was refrigerated at 4 °C for 48 h and then added to a solid  $\text{CO}_2$ -acetone-cooled suspension of the lithium salt of *t*-butyl peroxide (0.001 mol) in diethyl ether (25 ml). [The latter was prepared by the addition of a solution of *n*-butyllithium (0.64 g, 0.001 mol) in *n*-hexane (0.65 ml) to a solid  $\text{CO}_2$ -acetone-cooled solution of *t*-butyl hydroperoxide (0.09 g, 0.001 mol) in sodium-dried diethyl ether (25 ml).] The stirred reaction mixture was slowly brought to room temperature and heated under reflux for 5 min. After being cooled it was poured into ice-cooled aqueous sulphuric acid (10%; 100 ml) and the ethereal phase was washed with water ( $3 \times 50$  ml) before extraction with aqueous sodium hydroxide (10% w/v;  $3 \times 50$  ml). The combined extracts were acidified with sulphuric acid and extracted with diethyl ether ( $3 \times 50$  ml). The combined ethereal extracts were evaporated under reduced pressure to give a residue of a trimethoxydibenzofuranol which was purified by t.l.c. (5% EtOH— $\text{CHCl}_3$ ). Thus, 1,2,3-trimethoxydibenzofuran-4-ol (13), 1,2,4-trimethoxydibenzofuran-3-ol (12), and 1,3,4-trimethoxydibenzofuran-2-ol (11) were all prepared in low yields by this method. Attempts to prepare 2,3,4-trimethoxydibenzofuran-1-ol (10) failed. In all cases more than 70% of the trimethoxydibenzofuran starting material was recovered.

1,2,3-Trimethoxydibenzofuran-4-ol (13) (46 mg, 17%) was obtained as rhombic prisms, m.p. 112.5—114 °C (from diethyl ether) (Found:  $M^+$ , 274.0850.  $\text{C}_{15}\text{H}_{14}\text{O}_5$  requires  $M$ , 274.0841);  $\lambda_{\text{max}}$  (EtOH; 1 cm) 220 (log  $\epsilon$  4.50), 231 (4.50), 262 (4.11), 285 (4.22), and 304 nm (3.75);  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ; 0.1 mm) 3 527m (OH), 3 050w, 3 025w, 3 000w (Ar), 2 974w, 2 934m, 2 870w, 2 830w ( $\text{CH}_3$ ), 1 602m, 1 498m (Ar), 1 458m, 1 447s, 1 420s (Ar and  $\text{CH}_3$ ), 1 377m, 1 248m, 1 058s, and 1 043s (C—OH and C—O—C);  $\delta_{\text{H}}$  (90 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 3.95, 3.99, and 4.02 (each 3 H, s, together 1-, 2-, and 3-OMe), 5.72 (1 H, br s, 4-OH), 7.15—7.57 (3 H, m, 6-, 7-, and 8-H), and 7.93—8.08 (1 H, m, 9-H);  $m/z$  (e.i., 40 eV) 275 (18.4%), 274 ( $M^+$ , 100), 260 (15.8), 259 (94.4), 244 (17.0), 216 (37.2), 213 (16.8), 201 (37.7), 173 (28.8), 145 (17.2), 144 (12.5), 137 (13.0), 101 (10.0), 89 (27.7), and 88 (14.3);  $R_{\text{F}}$  (1.5% EtOH— $\text{CHCl}_3$ ) 0.37, [20%  $(\text{CH}_3)_2\text{CO}$ — $n$ - $\text{C}_6\text{H}_{14}$ ] 0.21.

1,2,4-Trimethoxydibenzofuran-3-ol (12) (31 mg, 11%) was an oil (Found:  $M^+$ , 274.0834);  $\lambda_{\text{max}}$  (EtOH; 1 cm) 220 (log  $\epsilon$  4.42), 229 (4.42), 261 (4.02), 289 (4.18), and 300sh nm (4.05);  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ; 0.1 mm) 3 512m (OH), 3 050w, 3 020w, 3 000w (Ar), 2 932m, 2 830w ( $\text{CH}_3$ ), 1 630w, 1 600m, 1 500m (Ar), 1 460m, 1 448s, 1 410s (Ar and  $\text{CH}_3$ ), 1 345m, 1 298m, 1 263m, 1 058s, and 1 036s  $\text{cm}^{-1}$  (C—OH and C—O—C);  $\delta_{\text{H}}$  (90 MHz;  $\text{CDCl}_3$ ;  $\text{Me}_4\text{Si}$ ) 3.97, 4.03, and 4.15 (each 3 H, s, together 1-, 2-, and 4-OMe), 5.93 (1 H, br s, 3-OH), 7.14—7.57 (3 H, m, 6-, 7-, and 8-H), and 7.89—8.05 (1 H, m, 9-H);  $m/z$  (e.i., 40 eV) 275 (19.5%), 274 ( $M^+$ , 100), 260 (15.9), 259 (90.2), 244 (17.8), 229 (12.1), 216 (35.3), 213 (24.1), 201 (39.3), 173 (26.3), 145 (19.2), 101 (10.2), 89 (25.0), and 88 (12.5);  $R_{\text{F}}$  (1.5% EtOH— $\text{CHCl}_3$ ) 0.40, [20%  $(\text{CH}_3)_2\text{CO}$ — $n$ - $\text{C}_6\text{H}_{14}$ ] 0.22;  $R_{\text{f}}$  g.l.c. 7.3 min;  $R_{\text{f}}$  h.p.l.c. (System 1) 25.4 min. Cf. the data for  $\beta$ -pyrufuran above.

1,3,4-Trimethoxydibenzofuran-2-ol (11) (15 mg, 5%) was an oil (Found:  $M^+$ , 274.0823);  $\lambda_{\text{max}}$  (EtOH; 1 cm) 224 (log  $\epsilon$  4.37), 260 (4.06), 288 (4.17), and 316sh nm (3.50);  $\nu_{\text{max}}$  (CHCl<sub>3</sub>; 0.1 mm) 3 520m (OH), 3 050w, 3 025w, 3 000w (Ar), 2 933m, 2 830w (CH<sub>3</sub>), 1 600m, 1 505m (Ar), 1 457m, 1 450s, 1 410s (Ar and CH<sub>3</sub>), 1 370m, 1 298m, 1 265s, 1 063s, and 1 040s cm<sup>-1</sup> (C-OH and C-O-C);  $\delta_{\text{H}}$  (90 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 4.03, 4.05, and 4.15 (each 3 H, s, together 1-, 3-, and 4-OMe), 5.55 (1 H, br s, 2-OH), 7.16–7.57 (3 H, m, 6-, 7-, and 8-H), and 7.95–8.12 (1 H, m, 9-H);  $m/z$  (e.i, 40 eV) 275 (18.3%), 274 ( $M^+$ , 89.0), 260 (17.9), 259 (100), 244 (12.1), 216 (39.4), 213 (22.4), 201 (36.7), 173 (26.2), 145 (20.0), 144 (11.9), 89 (26.2), and 88 (14.7);  $R_{\text{F}}$  (1.5% EtOH-CHCl<sub>3</sub>) 0.38, [20% (CH<sub>3</sub>)<sub>2</sub>CO-n-C<sub>6</sub>H<sub>14</sub>] 0.22;  $R_{\text{t}}$  g.l.c. 7.3 min;  $R_{\text{t}}$  h.p.l.c. (System 1) 23.4 min. Cf. the data for  $\alpha$ -pyrufuran, above.

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